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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,014	PROUDFOOT ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 6 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A. Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 9, drawn to isolated polypeptides of mutant chemokine molecules, classified in class 530, subclass 324.

2. In addition, claim 9 is subject to further restriction. The claim is drawn to a number of structurally and functionally distinct polypeptides (SEQ ID NO: 1-9). **In order to be fully responsive**, Applicant is required to further select a specific polypeptide. This is NOT an election of species. The claimed polypeptides are structurally distinct chemical compounds, and are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such polypeptide is presumed to represent an independent and distinct invention, subject to restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141.

3. Claims 6-8 and 10-12 link(s) claim 9. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 6-8 and 10-12. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

4. In a telephone call on 08/11/2005 with Dr. Frank C. Eisenschenk, Applicants elected, with traverse, SEQ ID NO:1 of claim 9. Applicant's election of SEQ ID NO:1 with traverse is acknowledged. The traverse is on the grounds that SEQ ID NOs:1-7 read on sequences that are 90% homologous, and thus would not represent a serious search burden for the Office. The Applicant's arguments have been fully considered and are not found to be persuasive. Although the polypeptides of SEQ ID NO:1-7 are 90% homologous, they are separate and distinct polypeptides, and are thus considered to be separate and distinct inventions. Searching all of the sequences would therefore represent a serious search burden on the Office. The requirement is still deemed proper and is therefore made FINAL.

B. *Priority*

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 02100339.7, filed on 04/04/2002.

C. Information Disclosure Statement

The information disclosure statement filed on 07/11/2005 has been entered in to the record, and has been fully considered.

D. Claim Objections

1. Claim 9 is objected to because it recites non-elected subject matter, namely the polypeptides of SEQ ID NO:2-9.

E. *Claim Rejections - 35 USC § 112, first paragraph – enablement*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising the amino acid sequence of SEQ ID NO:1, does not reasonably provide enablement for polypeptides with at least 90% homology to the corresponding wild-type molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

1. Claims 6-8 and 10-12 are drawn to isolated polypeptides or polynucleotides encoding mutant chemokines of RANTES, MIP-1α, and MIP-1β, and their muteins, having at least 90%, or 95-99%, homology with the corresponding wild-type molecule. While being enabling for SEQ ID NO:1, the specification does not provide enablement for polypeptides or polynucleotide having at least 90%, or 95-99% homology, to the corresponding wild-type molecules. The specification does not enable any person skilled in the art to which it pertains to make the invention commensurate in scope with these claims. There is no functional limitation in the claims, which encompass an unreasonable number of inoperative polypeptides, or polynucleotides that encode these polypeptides, which a person of ordinary skill in the art would no know how to use. Additionally, the claims recite muteins of the mutant chemokines. In the absence of a definition from the specification, the term "mutein" has been interpreted by the examiner to mean "mutant". Therefore, the Applicant's are claiming mutants of the chemokine mutants. The specification does not teach, describe, or provide any examples of mutant chemokines that have been further mutated and have at least 90%, or 95-99% homology, to the wild-type molecules.

There are no working examples in the specification of polypeptides less than 100% identical to the wild-type molecules, other than that of SEQ ID NO:1. A person of ordinary skill in the art would not know how to make polypeptides or polynucleotides with 90% or greater homology to the wild-type sequences, and would lack knowledge about the function(s) of such polypeptides or polynucleotides. Without a clear delineation of encompassed mutations, a skilled artisan could not know if the mutated chemokine polypeptides are operable within the present invention. It is well known in the art that single amino acid changes can severely affect polypeptide function. Luck *et al* have reported that even conservative amino acid changes can alter polypeptide activity by as much as 90% (Luck *et al*, Molec. Endocrinol, Vol 5(12), p 1880-1886. In particular, see p. 1881, Table 1). Thus, changes in primary amino acid sequence can affect both tertiary structure and function of polypeptides, and it is not possible for one of ordinary skill in the art to know if the broad claim of the recited mutant chemokine polypeptides can be used in the instant invention. It would not be predictable to one of ordinary skill in the art which residues would be critical for polypeptide or polynucleotide function, and which can be altered and still maintain the functional characteristics of the protein or nucleic acid, and therefore a skilled artisan would require undue experimentation in order to use the invention commensurate with the scope of the claims. Furthermore, a skilled artisan would be unable to predict how to further mutate a chemokine mutant (i.e. a mutein) while still retaining necessary structural and functional characteristics without undue experimentation. For these reasons, which include the complexity and unpredictability inherent in the claimed invention and the art, the lack of direction, guidance, or working examples for using polypeptides or polynucleotides other than SEQ ID NO:1 that are at least 90% homologous to the wild-type peptides, and the breadth of the claims, which can essentially encompass any polypeptide or polynucleotide with at least 90% homology to the wild-type chemokine, which could potentially be millions of polypeptides. The Examiner holds that undue experimentation would be required to practice the invention as claimed.

2. Claims 6-8 and 10-12 are drawn to chemokine mutants comprising "at least one non-conservative mutation in the 40's dibasic site." The specification, while enabling for a mutation defined by SEQ ID NO:1, is not enabling for other mutations of the 40's dibasic site, or mutations of other, non-40s dibasic site amino acids. The specification does not teach which residues must be mutated, and with which amino acid the residues must be mutated to, in order

to use the invention commensurate with the scope of the claims. As written, the claims read broadly on any mutation of the wild-type molecule, with at least one mutation occurring in the 40's dibasic site, and with any number of residues within the site mutated in a non-conservative manner. In theory, every amino acid residue in the wild-type molecule can be altered. It would not be predictable to a skilled artisan which amino acid residues, or combinations of amino acid residues, can be mutated and still retain the desired structure and function of the resulting polypeptide or polynucleotide. The specification provides no guidance, or working examples of any 40's dibasic site mutations other than that of SEQ ID NO:1. Thus, a person of ordinary skill in the art would not be able to conceive of any chemokine mutants with at least one mutation in the 40's dibasic site that would have the desired function of the claimed invention. Due to the breadth of the claims, the lack of predictability of the art and the invention, and the lack of guidance or working examples, a skilled artisan would require undue experimentation to use the invention commensurate with the claims.

3. Claim 8 is drawn to an isolated mutant polypeptide containing alanine or glutamic acid "in at least one of the positions of the 40's dibasic site." As stated in the above paragraph, the specification is enabling only for the polypeptide defined by SEQ ID NO:1. The specification is not enabling for mutants characterized by mutation to alanine or glutamic acid in any position within the 40's dibasic site, other than that defined by the polypeptide of SEQ ID NO:1. The specification does not teach, or provide any examples of, mutants which contain alanine or glutamic acid in any position of the 40's dibasic site, except that which is defined by SEQ ID NO:1. It would not be predictable to a skilled artisan which amino acid residues to mutate to alanine or glutamic acid and still retain the desired structure and function of the polypeptide. A person of ordinary skill in the art would only know how to make and use the polypeptide of SEQ ID NO:1, and would not be able to predict the biological activity or function of any other mutant chemokine molecule without undue experimentation. Therefore, because of the breadth of the claim, the lack of guidance or examples in the specification, and the unpredictability of the art, a skilled artisan would not know how to make or use a chemokine mutant, other than that of SEQ ID NO:1, with an alanine or glutamic acid mutation in any of the positions of the 40's dibasic site, without undue experimentation.

F. Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 6-8 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

1. Claims 6-8 and 10-12 are drawn to polypeptides or polynucleotides with at least 90%, or 95-99%, homology to the wild-type molecules. The claims do not require that the polypeptides or polynucleotides of the present invention posses any particular biological activity, or other distinguishing feature other than having at least 90%, or 95-99% homology to the wild-type molecule. Thus, Applicants are claiming a genus of polypeptides and polynucleotides that is defined only by sequence similarity.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicants have only described the polypeptide of SEQ ID NO:1. The specification does not provide adequate written description for any polypeptide with at least 90%, or 95-99% homology to the wild-type molecule. The specification does not describe what changes can be made while maintaining the desired structure and function of the wild-type molecules. Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:1, or polynucleotides that encode SEQ ID NO:1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

2. Claims 6-8 and 10-12 are drawn to an isolated polypeptide (or polynucleotide – claim 11) comprising a mutant C-C chemokine of RANTES, MIP-1α, and MIP-1β "*and their muteins*", having at least 90%, or 95-99% homology to the wild-type molecule. As stated above in section E.1, the examiner as interpreted the term "mutein" to mean "mutant". As written, the claims read on mutants of chemokine mutants, and the Applicant's are therefore claiming a genus of polypeptides or polynucleotides that are not adequately described in the specification. The specification does not provide any structural or functional description of such muteins, other than they must be at least 90%, or 95-99% homologous to the wild-type molecule. The specification does not provide adequate written description for any amino acids or nucleic acids that are further mutated in a chemokine mutant and still retain the structure and function of the original mutant or the wild-type molecule. The Applicant's are therefore claiming a genus of polypeptides and polynucleotides that is defined only by sequence identity, and as set forth in *Vas-Cath Inc. v. Mahurkar* (see above), does not meet the written description guidelines for 35 U.S.C. 112, first paragraph.

3. Claims 6-8 and 10-12 are drawn to chemokine mutants comprising "at least one non-conservative mutation in the 40's dibasic site." As written, the claims do not require that the polypeptides or polynucleotides of the present invention posses any particular biological activity, or other distinguishing feature other than a non-conservative mutation of the 40's dibasic site. The Applicant's have only described the polypeptide of SEQ ID NO:1, and the specification does not provide written description for any chemokine mutant with a non-conservative mutation in the 40s dibasic site, other than that of SEQ ID NO:1. Thus, Applicant's are claiming a genus

of polypeptides and polynucleotides that is defined only by sequence identity, and as set forth in *Vas-Cath Inc. v. Mahurkar* (see above), does not meet the written description guidelines for 35 U.S.C. 112, first paragraph.

4. Claim 8 is drawn to an isolated mutant polypeptide containing alanine or glutamic acid "in at least one of the positions of the 40's dibasic site." The claim does not limit the position, or the number, of any potential mutations. The specification only teaches the polypeptide of SEQ ID NO:1, and does not describe the structural or functional characteristics of other chemokine mutants containing alanine or glutamic acid in the 40s dibasic site, and does not teach which amino acids can be mutated to alanine or glutamic acid and still retain the desired structure and function. Therefore, Applicants are claiming a genus of polypeptides and polynucleotides that is defined only by sequence identity, and as set forth in *Vas-Cath Inc. v. Mahurkar* (see above), does not meet the written description guidelines for 35 U.S.C. 112, first paragraph.

G. Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 6-7, and 10-12 are drawn to an isolated polypeptide (or polynucleotide – claim 11) comprising a mutant C-C chemokine of RANTES, MIP-1α, and MIP-1β *and their muteins*". The claims are vague and indefinite because the intended use of the term "muteins" is not clear. As written, the claims read on mutants of RANTES, MIP-1α, MIP-1β, and also mutants of their muteins. The specification does not define the term "mutein", which has been interpreted by the Examiner to mean mutant. The specification also does not state which muteins the mutant polypeptides are derived from. The claims, therefore, fail to particularly point out and distinctly

claim essential subject matter that the Applicants regard as the invention. Claims 8 and 9 are rejected because they depend from rejected base claims.

H. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 6-8 and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Lusso and Polo (WO 99/33989). The claims of the instant application are drawn to isolated mutant chemokine polypeptides having at least one mutation in the 40s dibasic site and having at least 90% homology to the wild-type molecules, and to polynucleotides encoding the mutant polypeptides. The instant application also claims a pharmaceutical composition of said mutants, and a method of administering the composition to an individual. Lusso and Polo teach mutants of the chemokine RANTES, with said mutations occurring in the 40s dibasic site. Specifically, Lusso and Polo teach mutation of Arg 44, Lys 45, and Arg 46 (p 3, lines 4-25, and claims 1-4, 7)). Furthermore, Lusso and Polo specifically teach mutation of Arg 44, Lys 45, and Arg 46 to Alanine (p 3, lines 12-14 and 21-25, and also claim 4). While Lusso and Polo does not specifically disclose the percent identity to the wild-type molecules, it is noted that the peptides are mutated with respect to the wild-type molecule (p 3, lines 4-6), which is a polypeptide of 91 amino acids (Schall *et al*, 1988, J.Immunol., Vol. 141, p. 1018-1025. Note: Schall *et al* is not being used as grounds for rejection of any claim, but to point out an inherent feature of the wild-type RANTES polypeptide). A RANTES mutated at one amino acid would still be 99% homologous (90/91 = 98.9%, which would be rounded up to 99% because the claims only require 2 significant figures) to the wild-type at the level of amino acid sequence, and would therefor meet the limitations of claim 7 of the instant application. Similarly, mutation of 3 amino acids relative to the wild-type molecule would still result in a molecule with at least 90% homology (88/91 = 96.7%) to the wild-type molecule at the level of amino acid sequence, thus meeting the limitation of claim 6 of the instant application. For reasons discussed above, claim 8 of the instant application is taught by Lusso and Polo. Lusso and Polo also teach

polynucleotides encoding the RANTES mutants (p 4, lines 24-25, and claim 15), thus anticipating claim 11 of the instant application, and a pharmaceutical composition of the RANTES mutants (p 5, lines 17-22, and claim 17), which meets the limitations of claim 10 of the instant application.

2. Claims 6-9, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Proudfoot et al (J. Biol. Chem., Vol. 276, p. 10620-10626, published online on 12/14/2000). The claims of the instant application are drawn to isolated mutant chemokine polypeptides having at least one mutation in the 40s dibasic site and having at least 90% homology to the wild-type molecules, and to polynucleotides encoding the mutant polypeptides. Proudfoot *et al* teaches mutant RANTES polypeptides produced by mutating amino acid residues of the 40s dibasic region, including Arg 44, Lys 45, and Arg 47 (p. 10621, Experimental Procedures – *Generation of Nonheparin-binding Mutants*, and p. 10622, Table I). While the reference is silent regarding the percent identity to wild-type RANTES, which is a polypeptide of 91 amino acids, a RANTES polypeptide mutated at one amino acid would still be 99% homologous (90/91 = 98.9%, which would be rounded up to 99% because the claims only require 2 significant figures) to the wild-type at the level of amino acid sequence, and would therefor meet the limitations of claim 7 of the instant application. Similarly, mutation of 3 amino acids relative to the wild-type molecule would still result in a molecule with at least 90% homology (88/91 = 96.7%) to the wild-type molecule at the level of amino acid sequence, thus meeting the limitation of claim 6 of the instant application. Proudfoot *et al* also teach mutation of amino acid residues of the 40s dibasic region, wherein the mutated residue is mutated to alanine, and thus anticipates claim 8 of the instant application. In addition, Proudfoot *et al* teaches an R44A-K45A-R47A triple mutant, which meets the limitation of claim 9 of the instant application, which reads on SEQ ID NO:1, which consists of an R44A-K45A-R47A RANTES mutant polypeptide. Furthermore, the mutant polypeptides taught by Proudfoot *et al* were generated by PCR-based mutagenesis, which would produce polynucleotides encoding the mutant polypeptides. Therefore, Proudfoot *et al* also anticipates claim 11 of the instant application.

I. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lusso and Polo (WO 99/33989), in view of Strieter *et al* (US Patent No. 5,871,723). The present application is drawn to chemokine mutants of the 40s dibasic region, and a method of oral administration of these mutants. Lusso and Polo describe RANTES polypeptide mutants of the 40s dibasic region (see section 7.1 above), and their use in a pharmaceutical composition for administration to an individual; however, the reference is silent on a method of oral administration of the pharmaceutical composition. Strieter et al describe pharmaceutical compositions of chemokines for use in inhibiting angiogenesis, and further disclose oral administration as of method of administering the chemokines (column 6, lines 41-53, column 14, lines 31-49, and column 47, line 37 – column 48, line 20). It would have been obvious to one skilled in the art to combine the invention of Lusso and Polo, since they already teach a pharmaceutical composition of RANTES polypeptide mutants, with the methods of Strieter, et al, which describes methods of oral administration of chemokines. In addition, pharmaceutically acceptable carriers for use in oral administration are commonly available, and have long been known in the art. Indeed, oral administration is common for many therapeutic agents. A person of ordinary skill in the art would have a reasonable expectation of success in combining the chemokine mutants of Lusso and Polo, with the methods of oral chemokine administration disclosed by Strieter *et al*, and commonly know pharmaceutical carriers for oral administration, to practice the claimed invention of claim 12 of the instant application.

J. Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-12 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-5 and 9 of copending Application No. 10/398457. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: The subject matter of the instant application, and of application 10/398457 is drawn to polypeptide and polynucleotide mutants of the chemokine RANTES, with the mutations occurring in the 40's dibasic site in order to create a mutant chemokine with reduced glycosaminoglycan binding activity, and use as an oral therapeutic to treat human disease. Therefore, it would be expected that the RANTES mutants of Application No. 10/398457 would be at least 99% identical to the RANTES mutants of the instant application. In particular, claim 5 of Application No 10/389457 is drawn to the polypeptide of SEQ ID NO:3, which is 100% identical to SEQ ID NO:1 of the instant application (see sequence comparison).

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

K. Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached on M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER